REMARKS/ARGUMENTS

These Remarks are responsive to the Office Action mailed September 12, 2005 ("Office Action"). Claims 5-6, 9-14, 16-18, 29-31, 35-36, 39, and 42-43 are pending in the application. Applicant respectfully requests reconsideration of the rejection of the pending claims for the following reasons. In the Advisory Action dated March 8, 2006, Examiner Steadman indicated that claim 29 as amended is indefinite. In response, claim 29 is not limited to "naturally produced" in that it clearly encompasses utilization of recombinant organisms. Accordingly, a person of ordinary skill in the art at the time of the invention would not be confused as to the scope of claim 29.

Written Description -- 35 U.S.C. § 112, first paragraph

The Office Action rejects claims 9, 29-31, and 39 under 35 U.S.C. § 112, first paragraph, for lack of written description.

The Office Action states at page 3: "While it is acknowledged that the specification discloses representative species of media comprising chymosin and glucoamylase activities, these media appear to be obtained from microbial sources . . . . The disclosed media do not appear to be obtained from an animal species, a plant species, or a mammalian species." Claim 9 as amended states that "the medium having a pH of 2.0 or higher is derived from the cultivation of an organism that is selected from the group consisting of a bacterial species, a yeast species and a species of filamentous fungi." Applicant submits that the removal of "animal species" and "plant species" from claim 9 overcomes the rejection of claim 9. Claim 29 has been amended to state that "the organism comprises a gene encoding the chymosin activity that is derived from a mammalian species selected from the group consisting of a ruminant species, a *Camelidae* species, a porcine species, an *Equidae* species and a primate species." Applicant submits that this overcomes the Examiner's concern over whether certain ruminant species can endogenously express glucoamylase activity and whether the medium comprising chymosin and glucoamylase activity is obtained from the recited animal species. Accordingly, the rejection of claims 9, 29-31, and 39 under 35 U.S.C. § 112, first paragraph, for lack of written description must be withdrawn.

Enablement -- 35 U.S.C. § 112, first paragraph

The Office Action rejects claims 9, 29-31, and 39 under 35 U.S.C. § 112, first paragraph, for lack of enablement. Applicant submits that the claim amendments to claims 9 and 29 render this ground of rejection moot for the same reasons that they render the rejection for lack of written description moot. Accordingly, the rejection of claims 9, 29-31, and 39 under 35 U.S.C. § 112, first paragraph, for lack of enablement must be withdrawn.

Obviousness -- 35 U.S.C. § 103

The Office Action rejects claims 1, 5-6, 9, 12-14, 16-18, 29-31, and 42-43 under 35 U.S.C. § 103 as being unpatentable over Ward in view of Larsen.

"To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." Manual of Patent Examining Procedure § 2143.03 (8th ed., rev. 2, May 2004) (hereinafter "M.P.E.P."). "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." M.P.E.P. § 2112 (quoting Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)). "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." Id. (citing In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993), which reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art).

Both Ward and Larsen are discussed in the specification. Ward is discussed at page 2, lines 19-23. Larsen is discussed at page 3, lines 19-21.

Ward teaches improved production of chymosin in *Aspergillus* by expression of a glucoamylase-chymosin fusion protein. See Ward, Title & Abstract. In particular, Ward teaches

that the glucoamylase-chymosin fusion proteins can be secreted at higher efficiency compared to prochymosin. Ward, page 438, col. 1, last paragraph. Ward teaches that lowering the pH to 2 converts the fusion protein to chymosin and at least some pseudochymosin. Ward, page 439, col. 2, first paragraph. Ward teaches that "[p]resumably, this would eventually be further processed to mature chymosin under appropriate conditions." Ward, page 439, col. 2, first paragraph. Ward further teaches that "[p]seudochymosin is fairly stable at a pH below 3 or above 6 but is further processed to mature chymosin at pH 4.5." Ward, page 435, col. 1, first paragraph after the Abstract. Thus, Ward suggests raising the pH to 4.5 after activating the chymosin at a pH of 2.0 to convert any pseudochymosin to chymosin.

With respect to claim 1, the Office Action correctly acknowledges that Ward does not teach "practicing their method at a pH below 2.0." Office Action, page 18. Ward discloses that the inactive prochymosin can be processed at pH 2 to form pseudochymosin, which is further processed at pH 4.5 to obtain mature chymosin (Ward, col. 1) and he suggests that chymosin-glucoamylase hybrid protein might by processed the same way. Ward thus teaches the conversion of prochymosin into mature chymosin in a two step process with different pH optima. Starting with a solution having a neutral pH, Ward suggests lowering the pH to 2, but not lower as he shortly thereafter raises the pH to 4.5 in order to obtain mature chymosin.

Larsen discloses a method for purifying chymosin in its active form from an extract of animal stomach tissue, in which method the enzyme is claimed to be activated at a pH in the range of 0.5 to 5.0 for a period of time in the range of 10 to 120 minutes. Larson shows the optimum pH for adsorption of chymosin to the ion exchange matrix is about 2.0. See Larson, page 60, Table 11.1. Larson further teaches that the unwanted intermediate pseudochymosin is stable at low pH, but is processed to chymosin at higher pH, see Larson, page 2, line 19, which suggests raising the pH (conversion of prechymosin to pseudochymosin) in order to reduce costs.

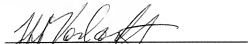
The teachings of Ward and Larson suggest that the pH of 2.0 is the optimal pH value for the combined activation and purification of chymosin, and there is therefore no motivation to use a pH of 2.0 as it will result in lower recovery and be more expensive. The Examiner is directed to M.P.E.P. § 2145.X.D.1-3, which discusses how proceeding against common wisdom is evidence of nonobviousness. Larsen is directed to purifying chymosin extracted from animal stomach tissue, while the claims now require the cultivation of an organism that is selected from

the group consisting of a bacterial species, a yeast species and a species of filamentous fungi. Finally, there is no discussion in Larsen of glucoamylase activity, let alone "reducing the glucoamylase activity in a milk clotting composition" as claimed.

"When evidence of secondary considerations such as unexpected results is initially before the Office, for example in the specification, that evidence should be considered in deciding whether there is a prima facie case of obviousness." M.P.E.P. § 2144.08. The Office Action has completely ignored the unexpected reduction of glucoamylase activity brought about by practicing the claimed process. Without benefit of having read Applicant's disclosure, a person of ordinary skill in the art could not foresee the reduction of glucoamylase activity brought about by practicing the claimed process. Instead of expecting to reduce glucoamylase activity, a person of ordinary skill in the art (without having knowledge of the Applicant's disclosure) would only expect to reduce the chymosin activity by lowering the pH below 2.0 (not the glucoamylase activity). Thus, neither Ward nor Larsen, alone or in combination, teach or suggest the claimed process of "reducing the glucoamylase activity in a milk clotting composition." Claim 9 is thus unobvious in view of the combined teachings of Ward and Larsen. Claims 5-6, 9-14, 16-18, 29-31, 35-36, and 42-43 are likewise unobvious as they depend from and incorporate the limitations of claim 9. Applicant also submits that the dependent claims deserve separate patentability consideration because they introduce limitations not found in either Ward or Larsen. Accordingly, the rejection of claims 5-6, 9-14, 16-18, 29-31, 35-36, and 42-43 under 35 U.S.C. § 103 must be withdrawn.

Applicant submits that this response addresses all of the issues raised in the Office Action and places the pending claims in condition for allowance. Should any issues remain to be discussed in this application, the undersigned may be reached by telephone. In the event any variance exists between the amount authorized to be charged to the Deposit Account and the Patent Office charges for reconsideration of this application, please charge or credit any difference to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,
HUNTON & WILLIAMS LLP

By: 
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